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SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: R GITOMER Examiner # : 69630 Date: 8/2/02
Art Unit: 1627 Phone Number 308 0532 Serial Number: 09/840,197
Mail Box and Bldg/Room Location: 3C19 Results Format Preferred (circle): PAPER DISK E-MAIL
7A11

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****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

_____

Earliest Priority Filing Date: _____

***For Sequence Searches Only** Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 - 703-305-4498
jan.delaval@uspto.gov

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STAFF USE ONLY	Type of Search		Vendors and cost where applicable	
Searcher:	NA Sequence (#)		STN	
Searcher Phone #:	AA Sequence (#)		Dialog	
Searcher Location:	Structure (#)		Questel/Orbit	
Date Searcher Picked Up: 8/30/02	Bibliographic	✓	Dr.Link	
Date Completed: 8/30/02	Litigation		Lexis/Nexis	
Searcher Prep & Review Time:	Fulltext		Sequence Systems	
Clerical Prep Time: 10	Patent Family		WWW/Internet	
Online Time: + 30	Other		Other (specify)	

PTO-1590 (8-01)

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Biotechnology & Chemical Library
CM1 1E07 - 703-308-4498
jan.delaval@uspto.gov

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               SET COST OFF

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L2             1 S ALPHA AND KERATOSE?
L3             1 S L1,L2

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L19            7 S E3,E4
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=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 13:41:24 ON 31 AUG 2002
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FILE COVERS 1907 - 31 Aug 2002  VOL 137 ISS 10
FILE LAST UPDATED: 30 Aug 2002  (20020830/ED)
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This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> d l23 all tot

L23 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:449430 HCAPLUS
DN 137:24288
TI Use of **alpha-keratose** as a **blood** plasma expander
IN **Widra, Abe**
PA USA
SO PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A01N043-04
ICS C12Q001-02
CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 9
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002045508	A1	20020613	WO 2001-US22727	20010718

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2000-254249P	P	20001208	
US 2001-840197	A	20010423	

AB A plasma expander and **blood** substitute comprising a therapeutic amt. of a soln. of .**alpha.-keratose**, a sol. fraction of keratin, as an oncotic agent with nutrient growth properties suitable as a transport vehicle for the natural or synthetically formed elements of **blood**. The soln. of .**alpha.-keratose** is non-antigenic, does not require **blood** typing, is free of disease producing viruses and may be stored indefinitely at ambient temps. in the lyophilized state. For example, the **blood** loss in severely stressed beagle dogs (**blood** loss of > 300 mL) was replaced with 300 mL of 2.5% .**alpha.-keratose** colloid (wt./vol.) in a crystalloid solvent Normosol R pH 7.4 during a 5.5 min time span without serious complications, thereby demonstrating the usefulness of .**alpha.-keratose** as an oncotic agent. At the conclusion of all testing, the dog was eating and looking quite strong, showing no ill effects from the expt. This expt. indicates that the .**alpha**.-**keratose** soln. of the present invention provides a useful transport medium for the formed cellular elements of **blood** and maintains normal vascular osmotic pressure due to its oncotic properties. A protein, the extn./genesis of which took place at refrigerator temp. (4.degree., to prevent possible heat denaturation) is not subject to freezing under the same condition. Indeed, 2.5% .**alpha.**-**keratose** in salt soln. does not freeze or become noticeably more

viscous from 12.degree. down to 2.degree., thereby allowing its use in hypothermic applications of the transfusion art, such as, but not limited to, open-heart surgery and organ transplantation.

ST keratose **blood** substitute organ preservation cell culture

IT **Blood** substitutes
Electrolytes, biological
Physiological saline solutions
(.**alpha**.-**keratose** soln. as **blood** plasma expander)

IT Salts, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.**alpha**.-**keratose** soln. as **blood** plasma expander)

IT **Blood** serum
(.**alpha**.-**keratose** soln. as **blood** plasma expander and for serum-free cell culture)

IT Animal tissue culture
(.**alpha**.-**keratose** soln. as **blood** plasma expander for growth of isolated cells)

IT Organ preservation
Preservation solutions (tissue)
(.**alpha**.-**keratose** soln. as **blood** plasma expander for maintaining isolated organ)

IT Mammalia
Shock (circulatory collapse)
(.**alpha**.-**keratose** soln. as **blood** plasma expander for treatment of mammal in shock)

IT Pathogen
Poisons, nonbiological source
(.**alpha**.-**keratose** soln. as **blood** plasma expander in removal of pathogens, poisons, and toxins from **blood**)

IT Toxins
RL: REM (Removal or disposal); PROC (Process)
(.**alpha**.-**keratose** soln. as **blood** plasma expander in removal of pathogens, poisons, and toxins from **blood**)

IT **Blood** cell
Blood transfusion
(.**alpha**.-**keratose** soln. as **blood** plasma expander in removal of pathogens, poisons, and toxins from **blood** and resuspending **blood** cells)

IT 50-99-7, Dextrose, biological studies 7647-14-5, Sodium chloride, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.**alpha**.-**keratose** soln. as **blood** plasma expander)

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Chunippon Seni Kogyo Kyodo Kumiai; JP 10077210 A 1998 HCAPLUS
(2) Ewald, R; Proceedings for the Society for Experimental Biology and Medicine 1964, V115(1), P130
(3) Segal; US 5698536 A 1997 HCAPLUS
(4) Taylor; US 5405742 A 1995 HCAPLUS
(5) University Of Illinois Foundation; EP 0089152 A1 1983 HCAPLUS

L23 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2002 ACS
AN 1985:427348 HCAPLUS
DN 103:27348
TI Hydrophilic biopolymeric copolyelectrolytes for biodegradable wound dressings
IN **Widra, Abe**
PA University of Illinois Foundation, USA

SO Eur. Pat. Appl., 33 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM A61L015-04
ICS A61L027-00; C08L089-00; C08L005-08
CC 63-7 (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 138385	A2	19850424	EP 1984-306266	19840913
EP 138385	A3	19870114		
EP 138385	B1	19900418		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
CA 1213521	A1	19861104	CA 1984-456295	19840611
AT 52034	E	19900515	AT 1984-306266	19840913
JP 60122568	A2	19850701	JP 1984-198384	19840921
JP 06014956	B4	19940302		
PRAI US 1983-534486		19830921		
EP 1984-306266		19840913		

AB Hydrogel membranes as biodegradable dressings for denuded tissue wound sites such as burn wounds and ulcerations, are water-insol., water-swellable materials comprising a water-sol. linear anionic polyelectrolyte component derived from keratin and a water-sol. linear cationic biopolymer polyelectrolyte component derived from at least 1 biopolymer consisting of a glucsaminoglycan such as chitosan and the protein collagen. In their hydrated form, the copolyelectrolytes are stress durable hydrogels which can be manipulated like a self-annealing paste or putty and thereby formed into membrane sheets. The copolyelectrolytes can be regenerated by the addn. of water from their dehydrated form to their hydrogen form, and reshaped. Thus, a chitosan collagen keratinate copolyelectrolyte was prepd. by mixing chitosan acetate 30, collagen acetate 10, and ammonium keratinate 10 mL to pptn. end-point. Upon evapn. of the supernatant, the ppt. dried to a cryst.-like sheet which upon addn. of water resulted in a hydrogel membrane. The effectiveness of a hydrogel membrane contg. gentamycin sulfate [1405-41-0] was demonstrated in a patient with multiple leg ulcers.

ST biopolymer copolyelectrolyte biodegradable wound dressing
IT Collagens, compounds
RL: BIOL (Biological study)
(acetates, complexes with ammonium keratinate and chitosan acetate, as biodegradable wound dressing)
IT Surgical dressings and goods
(biodegradable, chitosan-collagen keratinate copolyelectrolytes as)
IT Antibiotics
(chitosan-collagen keratinate copolyelectrolyte hydrogel wound dressing contg.)
IT Membrane, biological
(copolyelectrolyte hydrogels, as wound dressings)
IT Biopolymers
RL: BIOL (Biological study)
(copolyelectrolytes, as biodegradable wound dressings)
IT Polyelectrolytes
(anionic, biodegradable wound dressings)
IT Polyelectrolytes
(cationic, biodegradable wound dressings)
IT Gels
(hydro-, copolyelectrolytes, as wound dressings)
IT Surgical dressings and goods
(tubing, chitosan-collagen keratinate for)
IT **Keratins**
RL: BIOL (Biological study)

(.**alpha**.-**keratoses**, ammonium salts, complexes with chitosan and collagen acetates as biodegradable wound dressings)
IT 42617-20-9D, complexes with ammonium keratinate
RL: BIOL (Biological study)
(biodegradable wound dressings)
IT 127-33-3 1403-66-3 1405-41-0 35607-66-0 62893-20-3
RL: BIOL (Biological study)
(chitosan-collagen keratinate copolyelectrolyte hydrogel wound dressing contg.)

L23 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2002 ACS
AN 1983:581516 HCAPLUS
DN 99:181516
TI Hydrophilic bipolymeric copolyelectrolytes, and biodegradable wound dressings comprising them
IN **Widra, Abe**
PA University of Illinois Foundation, USA
SO Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DT Patent
LA English
IC A61L015-04; C08H001-00; C08B037-08
CC 63-7 (Pharmaceuticals)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 89152	A1	19830921	EP 1983-301149	19830303
	EP 89152	B1	19861015		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	CA 1213520	A1	19861104	CA 1983-421701	19830216
	AT 22805	E	19861115	AT 1983-301149	19830303
	FI 8300838	A	19830918	FI 1983-838	19830314
	FI 71944	B	19861128		
	FI 71944	C	19870309		
	DK 8301219	A	19830918	DK 1983-1219	19830316
	NO 8300934	A	19830919	NO 1983-934	19830316
	ES 520658	A1	19840501	ES 1983-520658	19830316
	JP 58170721	A2	19831007	JP 1983-45261	19830317
	JP 03047867	B4	19910722		
PRAI	US 1982-358994		19820317		
	EP 1983-301149		19830303		

AB Hydrophilic biopolymer polyelectrolytes prepd. from a water-sol. linear anionic protein polyelectrolyte component derived from keratin and a water-sol. linear cationic component from chitosans or collagen salts are useful as dressings for burn wounds. These polyelectrolyte membranes are rapidly, uniformly and strongly adherent to the underlying tissues by virtue of their shrinkdown from the fully hydrated state. In addn., they are durable to phys. stress and may be thickened and have a high degree of absorbent capacity for **blood** exudates. Collagen acetate was prepd. from collagen fibers by treatment with 0.25% HOAc. .**alpha**.-**Keratose** ammonium keratinate soln. was prepd. by treatment of human hair with water and peracetic acid for 24 h followed by removal of the acid. Washed hair was treated with 3N NH4OH and stirred for 24 h. The solubilized .**alpha**.-**keratose** ammonium keratinate was further purified and treated with collagen acetate soln. to yield a mixed soln. The soln. was evapd. to give a ppt. and the ppt. dried to give a cryst.-like sheet. On adding water to the ppt., a self-annealed diaphanous, flexuous cohesive collagen keratinate polyelectrolyte membrane was formed. The effectiveness of the membrane in wound healing was demonstrated in rabbits.
ST polymer polyelectrolyte membrane; wound dressing polymer polyelectrolyte; chitosan collagen surgical dressing
IT Collagens, compounds

RL: PREP (Preparation)
(acetates, reaction products with .**alpha.-keratose**
ammonium keratinate, prepn. of, for wound dressings)
IT Surgical dressings and goods
(chitosan or collagen salt reaction products with ammonium keratinate for)
IT Polyelectrolytes
(collagen or chitosan salt reaction products with ammonium keratinate, for wound dressings)
IT Membrane, biological
(polyelectrolyte polymer, for wound dressings)
IT **Keratins**
RL: BIOL (Biological study)
(.**alpha.-keratoses**, ammonium salts, reaction products with chitosan or collagen salts, for wound dressings)
IT 9012-76-4DP, reaction products with .**alpha.-keratose** ammonium keratinate 42617-20-9DP, reaction products with .**alpha.-keratose** ammonium keratinate
RL: PREP (Preparation)
(prepn. of, for wound dressings)

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FILE LAST UPDATED: 29 AUG 2002 <20020829/UP>
MOST RECENT DERWENT UPDATE 200255 <200255/DW>
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>>> The BATCH option for structure searches has been enabled in WPINDEX/WPIDS and WPIX <<<

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L46 ANSWER 1 OF 2 WPIX (C) 2002 THOMSON DERWENT
AN 1985-100548 [17] WPIX
CR 1983-772432 [39]
DNN N1985-075468 DNC C1985-043443
TI Keratin-collagen-glucosamino glycan membranes - for dressing **wounds.**
DC A96 D22 P34
IN **WIDRA, A**
PA (UNII) UNIV ILLINOIS FOUND
CYC 14
PI EP 138385 A 19850424 (198517)* EN 33p

R: AT BE CH DE FR GB IT LI NL SE
JP 60122568 A 19850701 (198532)
US 4570629 A 19860218 (198610)
CA 1213521 A 19861104 (198649)
EP 138385 B 19900418 (199016)
R: AT BE CH DE FR GB IT LI NL SE
DE 3481974 G 19900523 (199022)
JP 06014956 B2 19940302 (199412) A61L015-16

ADT EP 138385 A EP 1984-306266 19840913; JP 60122568 A JP 1984-198384 19840921; US 4570629 A US 1983-534486 19830921; JP 06014956 B2 JP 1984-198384 19840921

FDT JP 06014956 B2 Based on JP 60122568

PRAI US 1982-358994 19820317; US 1983-534486 19830921

REP A3...8702; EP 89152; GB 2026516; No-SR.Pub; US 4280954

IC A61L015-04; A61L027-00; A61M005-20; C07K015-02; C08L005-08; C08L089-00
ICM A61L015-16
ICS A61L015-04; A61L015-44; A61L017-00; A61L027-00; A61M005-20; C07K015-02; C08L005-08; C08L089-00

AB EP 138385 A UPAB: 19940510
Hydrophilic bipolymeric copolyelectrolytes used as biodegradable dressings for **wounds** are claimed which are an integral mixt. or layers of: (a) a water-soluble linear anionic protein polyelectrolyte derived from keratin, pref. ammonium ketatinate contg. **alpha-keratose** ; and (b) a water-soluble linear cationic biopolymer polyelectrolyte selected from a glucosaminoglycan (pref. chitosan) and collagen in a wt. ratio of 2:1-13:1 (pref. 0.001:1-1:1).

The dressings can opt. contain plasticisers or softeners (pref. glycerol) and an antibiotic. Membranes comprising at least 1 layer of a hydrogel formed from this compsn. are also claimed.

ADVANTAGE - The hydrogel membranes are strongly adherent to underlying tissues, elastic, permeable to O2 and water vapour, absorb **wound** exudates and are a barrier to bacteria.

Dwg.0/0

FS CPI GMPI

FA AB

MC CPI: A03-C01; A07-A01; A12-V03A; D09-C

ABEQ EP 138385 B UPAB: 19930925
A hydrophilic biopolymeric copolyelectrolyte of (a) a water-soluble linear anionic protein polyelectrolyte component derived from keratin, and (b) a water-soluble linear cationic biopolymer polyelectrolyte component derived from at least one biopolymer selected from a glucosaminoglycan and collagen, the weight ratio of said anionic protein polyelectrolyte component to said cationic biopolymer polyelectrolyte component lying within the range of from 0.001:1 to 16:1 but outside the range of from 1:1 to 10:1.

ABEQ US 4570629 A UPAB: 19930925
Novel hydrophilic biopolymeric copolyelectrolyte, comprises (a) a water-soluble linear anionic keratin-derived protein poly-electrolyte component; and (b) a water-soluble linear cationic biopolymer polyelectrolyte comprising glucosaminoglycan and/or collagen.

Pref. wt. ratio (a):(b) is 0.001-7:1 such that (a) is ammonium keratinate, and (b) is chitosan or chitosan/collagen in wt. ratio 0.5-13:1. Compsn. further comprises a flexibility- and/or adhesion-enhancing amt. of non-toxic plasticiser or softener (e.g. glycerol).

USE - As biodegradable dressings for denuded tissue **wound** sites.

L46 ANSWER 2 OF 2 WPIX (C) 2002 THOMSON DERWENT

AN 1983-772432 [39] WPIX

CR 1985-100548 [17]

DNN N1983-170058 DNC C1983-092450

TI Hydrophilic bio polymeric co polyelectrolytes - of water soluble linear

anionic protein polyelectrolyte derived from keratin and water soluble linear cationic bio polymer.

DC A11 A96 P32 P34
IN **WIDRA, A**
PA (UNII) UNIV ILLINOIS FOUND
CYC 19
PI EP 89152 A 19830921 (198339)* EN 24p
R: AT BE CH DE FR GB IT LI LU NL SE
JP 58170721 A 19831007 (198346)
NO 8300934 A 19831010 (198347)
DK 8301219 A 19831114 (198401)
FI 8300838 A 19831130 (198403)
PT 76405 A 19840315 (198416)
ES 8404392 A 19840716 (198438)
EP 89152 B 19861015 (198642) EN
R: AT BE CH DE FR GB IT LI LU NL SE
DE 3366839 G 19861120 (198648)
CA 1213520 A 19861104 (198649)
JP 03047867 B 19910722 (199133)
ADT EP 89152 A EP 1982-301149 19820303; JP 03047867 B JP 1983-45261 19830317
PRAI US 1982-358994 19820317; US 1983-534486 19830921
REP EP 38628; FR 2318189; FR 2332863; FR 2432046
IC A61F001-00; A61K015-04; A61K031-72; A61K037-12; A61L015-04; A61L027-00; A61M001-03; C08B037-08; C08H001-00; C08L089-00
AB EP 89152 A UPAB: 19940510
Hydrophilic biopolymeric copolyelectrolyte (I) of (a) a water soluble linear anionic protein polyelectrolyte component derived from keratin and (b) a water soluble linear cationic biopolymer polyelectrolyte component derived from a glucosaminoglycan and/or collagen is new.

Pref. (a) is ammonium keratinate(the keratin is esp. **alpha-keratose**); the glucosaminoglycan is chitosan, and (b) is a biopolymer carboxylate (esp. biopolymer acetate) or a mixt. of chitosan and collagen in wt. ratio 0.5-2:1. Pref. the wt. ratio of (a) to (b) is 1-10 (esp. 2-5):1.

(I) can be used in the form of hydrogel membranes, as biodegradable dressings, for burn **wounds** and other derived tissue **wound** sites. The dressing is adherent to derived tissues, elastic, durable and completely biodegradable so as to eliminate the necessity for its being stripped from the **wound** site. It is also adbsorbent to **wound** exudates without losing its durability and has water vapour characteristic sufficient to keep the underlying tissues moist without creating pooling.

Dwg.0/0
FS CPI GMPI
FA AB
MC CPI: A03-A; A03-C01; A12-M02; A12-V03A
ABEQ EP 89152 B UPAB: 19930925
A hydrophilic biopolymeric copolyelectrolyte of (a) a water-soluble linear anionic protein polyelectrolyte component derived from keratin and (b) a water-soluble linear cationic biopolymer polyelectrolyte component derived from at least one biopolymer selected from a glucosaminoglycan and collagen.

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DEL HIS
SET COST OFF

FILE 'REGISTRY' ENTERED AT 13:32:56 ON 31 AUG 2002
E .ALPHA.-KERATOSE/CN
L1 1 S E3

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L2              1 S ALPHA AND KERATOSE?
L3              1 S L1,L2

     FILE 'HCAOLD' ENTERED AT 13:34:58 ON 31 AUG 2002
L4              0 S L3

     FILE 'HCAPLUS' ENTERED AT 13:35:02 ON 31 AUG 2002
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L6            112 S (ALPHA OR ALFA)(S)KERATOSE
L7            114 S L5,L6
                  E KERATOSE/CT
                  E E3+ALL
L8             12 S E1(L)(ALPHA OR ALFA)
                  E E2+ALL
L9              5 S E6
L10            11 S E4(L)(ALPHA OR ALFA)
L11           117 S L7-L10
L12            81 S L11 NOT TEXTILE?/SC,SX,CW
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L14            18 S L13 NOT HAIR
L15             1 S L14 AND BLOOD
L16             2 S L11 AND BLOOD
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L18             1 S L17 NOT HAIR
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L19             7 S E3,E4
L20             3 S L19 AND L11
L21             3 S L18,L20
L22             4 S L19 NOT L21
L23             3 S L21 AND L5-L22
                  SEL RN

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L24             9 S E1-E9

     FILE 'HCAPLUS' ENTERED AT 13:41:24 ON 31 AUG 2002

     FILE 'BIOSIS' ENTERED AT 13:42:10 ON 31 AUG 2002
L25             1 S L3
L26            21 S L6
L27             2 S (ALPHA OR ALFA)()KERATOSE
L28            21 S L25-L27
                  E WIDRA A/AU
L29             7 S E3
L30             0 S L28 AND L29

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L31             0 S L1
L32             0 S L27
                  E KERATOSE/CT

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L33             2 S L1 OR L27

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L34             0 S L27

     FILE 'BIOBUSINESS' ENTERED AT 13:47:03 ON 31 AUG 2002
L35             0 S L1 OR L27

     FILE 'CBNB' ENTERED AT 13:47:29 ON 31 AUG 2002
L36             0 S L27
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L37           0 S L27

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L39           0 S L27

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L40           0 S L27

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L41           0 S L1 OR L27

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L42           6 S L27
L43           2 S L42 AND WOUND
L44           4 S L42 NOT L43
                E R12587+ALL/DCN
                E R01636+ALL/DCN
                E R01655+ALL/DCN
                E R01372+ALL/DCN
                E 9822-B4501+ALL/DCN
                E WIDRA A/AU
                E E3
L45           2 S E3
L46           2 S L43,L45
L47           8 S (ALPHA OR ALFA)()KERATIN

     FILE 'WPIX' ENTERED AT 13:57:06 ON 31 AUG 2002

=> fil uspatall
FILE 'USPATFULL' ENTERED AT 14:01:15 ON 31 AUG 2002
CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 14:01:15 ON 31 AUG 2002
CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

=> d bib ab hit tot l51

L51  ANSWER 1 OF 5  USPATFULL
AN     93:74190  USPATFULL
TI     Production of bioadhesive precursor protein analogs by genetically
       engineered organisms
IN     Maugh, Kathy J., Walnut, CA, United States
       Anderson, David M., Rockville, MD, United States
       Strausberg, Susan L., Silver Spring, MD, United States
       Strausberg, Robert, Silver Spring, MD, United States
       Wei, Tena, Rockville, MD, United States
PA     Enzon, Inc., Piscataway, NJ, United States (U.S. corporation)
PI     US 5242808              19930907
AI     US 1991-644745          19910123 (7)
DCD    20080917
RLI    Continuation of Ser. No. US 1987-25243, filed on 12 Mar 1987, now
       abandoned which is a continuation-in-part of Ser. No. US 1986-933945,
       filed on 24 Nov 1986, now abandoned which is a continuation-in-part of
       Ser. No. US 1984-650128, filed on 13 Sep 1984, now abandoned
DT     Utility
FS     Granted
EXNAM  Primary Examiner: Schwartz, Richard A.; Assistant Examiner: Mosher, Mary
       E.
LREP   Sterne, Kessler, Goldstein & Fox
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CLMN Number of Claims: 37
ECL Exemplary Claim: 1
DRWN 19 Drawing Figure(s); 19 Drawing Page(s)
LN.CNT 1993
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Recombinant production of bioadhesive precursor protein analogs is disclosed. The bioadhesive precursor protein analogs can be hydroxylated and used as an adhesive in wet environments.
DETD In a similar manner, other types of insoluble or crystalline protein sheets can be used as reinforcement for adhesive protein. For example, silk cloth, or sheets formed from solubilized and reprecipitated **alpha-keratose** from wool keratin fibers (J. De Bersagbes, Curr. Probl. Dermatol., 6:34-86 (1976)), or polymerized fibrin clot formed from purified fibrinogen, thrombin and Factor VIII (Redl, H. and G. Schlag, Facial Plastic Surgery, 2:315-321 (1985)) are used. For medical applications, the use of sheets of fibrin may have the additional benefit of helping to promote wound healing (Redl and Schlag, supra).

L51 ANSWER 2 OF 5 USPATFULL
AN 93:29134 USPATFULL
TI Bioadhesive precursor protein expression vectors
IN Maugh, Kathy J., Walnut, CA, United States
Anderson, David M., Rockville, MD, United States
Strausberg, Robert, Silver Spring, MD, United States
Strausberg, Susan L., Silver Spring, MD, United States
McCandliss, Russ, Gaithersburg, MD, United States
Wei, Tena, Rockville, MD, United States
Filpula, David, Gaithersburg, MD, United States
PA Enzon Labs, Inc., Gaithersburg, MD, United States (U.S. corporation)
PI US 5202256 19930413
AI US 1991-745695 19910816 (7)
RLI Division of Ser. No. US 1990-530449, filed on 30 May 1990, now patented, Pat. No. US 5049504 which is a continuation of Ser. No. US 1987-82456, filed on 7 Aug 1987, now abandoned which is a continuation-in-part of Ser. No. US 1986-933945, filed on 24 Nov 1986, now abandoned which is a continuation-in-part of Ser. No. US 1984-650128, filed on 13 Sep 1984, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Schwartz, Richard A.; Assistant Examiner: Mosher, Mary E.
LREP Sterne, Kessler, Goldstein & Fox
CLMN Number of Claims: 16
ECL Exemplary Claim: 1
DRWN 12 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 2797
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Vectors are provided that are capable of expressing, in microbial transformants, a protein having the native amino acid sequence of a bioadhesive precursor protein of a marine animal selected from the group consisting of mussels, barnacles, and oysters. The bioadhesive precursor protein can be expressed in transformants, recovered and converted to a bioadhesive protein by hydroxylation.
DETD In a similar manner, other types of insoluble or crystalline protein sheets can be used as reinforcement for adhesive protein. For example, silk cloth, or sheets formed from solubilized and reprecipitated **alpha-keratose** from wool keratin fibers (J. De Bersagbes, Curr. Probl. Dermatol., 6:34-86 (1976)), or polymerized fibrin clot formed from purified fibrinogen, thrombin and Factor VIII (Redl, H. and G. Schlag, Facial Plastic Surgery, 2:315-321 (1985)) are used. For medical applications, the use of sheets of fibrin may have the additional benefit of helping to promote wound healing (Redl and Schlag,

supra).

L51 ANSWER 3 OF 5 USPATFULL
AN 93:29116 USPATFULL
TI Method of producing bioadhesive protein
IN Maugh, Kathy J., Walnut, CA, United States
Anderson, David M., Rockville, MD, United States
Strausberg, Robert, Silver Springs, MD, United States
Strausberg, Susan L., Silver Springs, MD, United States
PA Enzon Labs Inc., Gaithersburg, MD, United States (U.S. corporation)
PI US 5202236 19930413
AI US 1990-528762 19900525 (7)
RLI Division of Ser. No. US 1987-82456, filed on 7 Aug 1987, now abandoned which is a continuation-in-part of Ser. No. US 1986-933945, filed on 24 Nov 1986, now abandoned which is a continuation-in-part of Ser. No. US 1984-650128, filed on 13 Sep 1984, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Schwartz, Richard A.; Assistant Examiner: Mosher, Mary E.
LREP Sterne, Kessler, Goldstein & Fox
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 13 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 1839
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Vectors are provided that are capable of expressing, in microbial transformants, a protein having the native amino acid sequence of a bioadhesive precursor protein of a marine animal selected from the group consisting of mussels, barnacles, and oysters. The bioadhesive precursor protein can be expressed in transformants, recovered and converted to a bioadhesive protein by hydroxylation.
DETD In a similar manner, other types of insoluble or crystalline protein sheets can be used as reinforcement for adhesive protein. For example, silk cloth, or sheets formed from solubilized and reprecipitated **alpha-keratose** from wool keratin fibers (J. De Bersagbes, Curr. Probl. Dermatol., 6:34-86 (1976)), or polymerized fibrin clot formed from purified fibrinogen, thrombin and Factor VIII (Redl, H. and G. Schlag, Facial Plastic Surgery, 2:315-321 (1985)) are used. For medical applications, the use of sheets of fibrin may have the additional benefit of helping to promote wound healing (Redl and Schlag, supra).

L51 ANSWER 4 OF 5 USPATFULL
AN 91:75651 USPATFULL
TI Bioadhesive coding sequences
IN Maugh, Kathy J., Walnut, CA, United States
Anderson, David M., Rockville, MD, United States
Strausberg, Robert, Silver Spring, MD, United States
Strausberg, Susan L., Silver Spring, MD, United States
McCandliss, Russ, Gaithersburg, MD, United States
Wei, Tena, Rockville, MD, United States
Filpula, David, Gaithersburg, MD, United States
PA Genex Corporation, Gaithersburg, MD, United States (U.S. corporation)
PI US 5049504 19910917
AI US 1990-530449 19900530 (7)
RLI Continuation of Ser. No. US 1987-82456, filed on 7 Aug 1987, now abandoned which is a continuation-in-part of Ser. No. US 1986-933945, filed on 24 Nov 1986, now abandoned which is a continuation-in-part of Ser. No. US 1984-650128, filed on 13 Sep 1984, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Schwartz, Richard A.; Assistant Examiner: Mosher, Mary

E.
LREP Sterne, Kessler, Goldstein & Fox
CLMN Number of Claims: 30
ECL Exemplary Claim: 1
DRWN 12 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 1865
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Vectors are provided that are capable of expressing, in microbial transformants, a protein having the native amino acid sequence of a bioadhesive precursor protein of a marine animal selected from the group consisting of mussels, barnacles, and oysters. The bioadhesive precursor protein can be expressed in transformants, recovered and converted to a bioadhesive protein by hydroxylation.
DETD In a similar manner, other types of insoluble or crystalline protein sheets can be used as reinforcement for adhesive protein. For example, silk cloth, or sheets formed from solubilized and reprecipitated **alpha-keratose** from wool keratin fibers (J. De Bersagbes, Curr. Probl. Dermatol., 6:34-86 (1976)), or polymerized fibrin clot formed from purified fibrinogen, thrombin and Factor VIII (Redl, H. and G. Schlag, Facial Plastic Surgery, 2:315-321 (1985)) are used. For medical applications, the use of sheets of fibrin may have the additional benefit of helping to promote wound healing (Redl and Schlag, supra).

L51 ANSWER 5 OF 5 USPATFULL
AN 86:8792 USPATFULL
TI Hydrophilic biopolymeric copolyelectrolytes, and biodegradable wound dressing comprising same
IN Widra, Abe, River Forest, IL, United States
PA University of Illinois Foundation, Urbana, IL, United States (U.S. corporation)
PI US 4570629 19860218
AI US 1983-534486 19830921 (6)
RLI Continuation-in-part of Ser. No. US 1982-358994, filed on 17 Mar 1982, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Rosenbaum, C. Fred; Assistant Examiner: Vinyard, Sherri E.
LREP Shimei, Barbara A.
CLMN Number of Claims: 39
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 919
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Hydrophilic biopolymeric copolyelectrolytes comprising (a) a water-soluble linear anionic protein polyelectrolyte component derived from keratin and (b) a water-soluble linear cationic biopolymer polyelectrolyte component derived from at least one biopolymer selected from the group consisting of collagen and a glucosaminoglycan. Hydrogel membranes formed from the copolyelectrolytes are useful as biodegradable dressings for denuded tissue wound sites.
SUMM The hydrophilic biopolymeric copolyelectrolytes of the present invention are water-insoluble, water-swellable materials comprising a water-soluble linear anionic protein polyelectrolyte component derived from keratin and a water-soluble linear cationic biopolymer polyelectrolyte component derived from at least one biopolymer selected from the group consisting of a glucosaminoglycan, such as chitosan, and the protein, collagen. Keratin is a protein obtained from sources such as skin, fur, hair, wool, horn, nails, claws, beaks, and scales. It may be readily isolated from its source material and separated into its **alpha-keratose** and gamma-keratose fractions by procedures well known in the art, such as, for example, as described by

Widra, Mycopathologia et Mycologia Applicata, Volume 30, pages 141-144 (1966) and Rhodes, et al., Mycopathologia et Mycologia Applicata, Volume 33, pages 345-348 (1967), incorporated herein by reference. Chitosan is the deacylated form of chitin, which is a glucosaminoglycan obtained as a major constituent of the shells of shrimp, crabs, and lobsters, the cell walls of filamentous fungi, and the exoskeletons of insects. Chitosan is commercially available in the form of fibers, for example, from Sigma-Aldrich Corporation, St. Louis, Mo. Collagen is a fibrous protein which comprises the major portion of the white fiber in connective tissues of the animal body, particularly in the skin, bones and tendons. It is commercially available in the form of soluble fibers, for example, from Sigma-Aldrich Corporation, St. Louis, Mo.

SUMM The water-soluble derivatives of keratin employed in the anionic polyelectrolyte component of the copolyelectrolytes of the present invention are linear polyelectrolytes in which the keratin moiety is in anionic form. A particularly suitable anionic keratin polyelectrolyte is ammonium keratinate, obtained as the total ammonium hydroxide-soluble fraction of peracetic acid-oxidized human hair, or the **alpha-keratose** component of this fraction, by the procedures described in the aforementioned Rhodes, et al., article. Due to evidence indicating a higher degree of nonantigenicity, the **alpha-keratose** form of ammonium keratinate is preferred.

DETD **Alpha-keratose** ammonium keratinate solution was prepared as follows. Twelve grams of clean, dry, blond human hair, previously degreased and washed, were placed in a 1 liter Erlynmeyer flask containing 320 ml of water. 80 ml of concentrated peracetic acid was added, and the flask stoppered. The contents of the flask were swirled and then placed in a refrigerator for 24 hours with occasional swirling. The bleached, easily stretched and torn ("retted") hair was then freed of the peracetic acid by decantation and thorough washing with separate water rinses. The washed retted hair was then covered with 800 ml of 3N ammonium hydroxide, and stirred in the cold for 24 hours to solubilize hair keratins. The total soluble protein (TP) fraction was then cleared of solids by centrifugation, and discarding undissolved protein and non-protein residual debris. The TP fraction was further clarified through Whatman No. 1 paper, dialyzed against water until the dialyzate wash gave only a faint positive for ammonia with Nessler's reagent, and then Seitz microfiltered. **Alpha-keratose** was precipitated from the TP fraction by incremental addition of 0.1 N hydrochloric acid while stirring. The precipitate was collected by centrifugation, and the supernatant gamma-keratose, antigenic for rabbits, was discarded. The **alpha-keratose** precipitate was washed in water, re-centrifuged, and then solubilized in 0.1N ammonium hydroxide. A second cycle of precipitation, washing, and solubilization was run on the **alpha-keratose** before final dialysis against water, concentration of the protein microfiltration, and storage in a sterile container. The resulting solution contained approximately 7.5 mg of **alpha-keratose** ammonium keratinate per ml.

DETD The collagen acetate and **alpha-keratose** ammonium keratinate stock solutions prepared in Example 1, were employed in the preparation of a collagen keratinate copolyelectrolyte. 10 ml of the collagen acetate solution (containing 20 mg of collagen acetate) and 10 ml of the ammonium keratinate solution (containing 75 mg of **alpha-keratose** ammonium keratinate) were mixed together in a plastic Petri dish to precipitation end-point. Upon evaporation of the supernatant, the precipitate dried down into a dry crystalline-like sheet. Upon adding water to the dried down precipitate, a self-annealed flexuous, diaphanous, cohesive collagen keratinate copolyelectrolyte hydrogel membrane was formed, which was teased and floated from the bottom of the dish.

DETD The chitosan acetate and **alpha-keratose** ammonium keratinate stock solutions prepared in Example 1, were employed in the preparation of a chitosan keratinate copolyelectrolyte. Fifty mg of chitosan acetate solution (containing 250 ml of chitosan acetate) and 15 ml of the ammonium keratinate solution (containing 112.5 mg of **alpha-keratose** ammonium keratinate), were mixed together in a plastic Petri dish to precipitation end-point to produce an opaque whitish, sticky, flocculent precipitate. Upon evaporation of the supernatant, the precipitate dried down to form a hard brittle translucent sheet, which was pried or cracked from the bottom of the dish. Upon adding water to the dried material, a self-annealed, tough, stretchable, cuttable, cohesive chitosan keratinate copolyelectrolyte hydrogel membrane was formed.

DETD All three of the stock solutions prepared in Example 1 were employed in the preparation of a chitosan-collagen keratinate copolyelectrolyte. 30 ml of the chitosan acetate solution (containing 150 mg of chitosan acetate), 10 ml of the collagen acetate solution (containing 20 mg of collagen acetate), and 10 ml of the ammonium keratinate solution (containing 75 mg of **alpha-keratose** ammonium keratinate), were mixed together in a plastic Petri dish to precipitation end-point. Upon evaporation of the supernatant, the precipitate dried down to a crystalline-like sheet. Upon adding water to the dried down precipitate, a self-annealed, flexible, cohesive chitosancollagen keratinate copolyelectrolyte hydrogel membrane was formed, which was teased and floated from the bottom of the dish.

DETD When the chitosan acetate sheeting was sprayed on both sides with a total of 10 ml (75 mg) of the **alpha-keratose** ammonium keratinate stock solution prepared in Example 1, the solid sheeting swelled to form a self-annealed, flexible, cohesive chitosan keratinate copolyelectrolyte hydrogel membrane.

DETD The 9".times.12" dried chitosan acetate sheeting was sprayed on both sides with a total of about 10 ml of a 5 mg/ml **alpha-keratose** ammonium keratinate solution prepared in a manner analogous to Example 1, to form a chitosan keratinate copolyelectolyte hydrogel membrane containing the representative antibiotic gentamycin sulfate.

DETD Seventy ml of this chitosan acetate solution was poured into a standard plastic Petri dish (3.5" diameter) and 300 mg demeclocycline powder (Declomycin, Lederle Laboratories Div. American Cyanamid Corp., Wayne, NJ) was added with stirring. The mixture was allowed to dry down to a membrane which was then lifted out and sprayed on both sides with a total of 3 ml of a 5 mg/ml **alpha-keratose** ammonium keratinate solution prepared in a manner analogous to that of Example 1, to form a chitosan keratinate copolyelectrolyte hydrogel membrane containing the representative antibiotic demeclocycline.

DETD Fifty eight ml of this chitosan acetate solution was poured into a standard plastic Petri dish and 1 ml glycerol and 320 mg cefoxitin powder (Mafoxin, Merck Sharp & Dohme, Rahway, NJ), were added with stirring. To this mixture was added 10 ml of a 5 mg/ml **alpha-keratose** ammonium keratinate solution prepared in a manner analogous to that of Example 1 and containing 125 mg of dissolved tetracycline (Sumycin, Squibb & Sons, Inc., Princeton, NJ). The combined mixture was allowed to dry down to a yellow-brown chitosan keratinate copolyelectrolyte hydrogel membrane containing the representative antibiotics cefoxitin and tetracycline.

DETD The 9".times.12" dried chitosan acetate sheeting was sprayed on both sides with a total of 10 ml of a 5 mg/ml **alpha-keratose** ammonium keratinate solution prepared in a manner analogous to Example 1 and containing 191 mg dissolved carbenicillin powder (Geocillin, Roerig Div. Pfizer Pharmaceuticals, New York, NY), to form a chitosan keratinate copolyelectrolyte hydrogel membrane containing the representative antibiotics gentamycin sulfate and carbenicillin.

DETD The ears of a ketamine-anaesthetized 10 pound male New Zealand white rabbit were shorn of hair and prepared for surgery. From the dorsal surface of one ear, a full thickness circle of skin 2.5 cm in diameter was removed, and the wound sponged dry. Sterile **alpha-keratose** ammonium keratinate solution prepared according to Example 1 was dropped into the wound area and on the surrounding shaven skin. A circular swatch of thin chitosan acetate sheeting (2.4 mg chitosan/cm.sup.2) was fitted over the wound area and surrounding skin, resulting in the formation of a chitosan keratinate copolyelectrolyte hydrogel membrane wound dressing, which became tightly bound to all surfaces in a few minutes of drying time. The area was dressed with sterile petrolatum gauze, bandaged and taped. A control ear was also prepared, wherein the wound was dressed only with sterile petrolatum gauze, bandaged and taped.

DETD A 10 pound female rabbit was prepared for surgery and a 3.5 cm diameter full thickness of skin was removed from the left flank. The site was then sprayed with sterile **alpha-keratose** ammonium keratinate solution prepared according to Example 1, and covered with a medium weight chitosan acetate sheet (3.6 mg chitosan/cm.sup.2), dressed with petrolatum gauze, bandaged, and taped.

DETD A 10 pound female rabbit was prepared for surgery, and a full thickness of skin removed from a rectangular area 2.5.times.3.5 cm.sup.2. After spraying the wound area with sterile **alpha-keratose** ammonium keratinate solution prepared according to Example 1, a double layer of chitosan acetate sheeting (two sheets annealed with **alpha-keratose** ammonium keratinate solution and containing a total of 6.4 mg chitosan/cm.sup.2) was applied to the wound and surrounding skin. The area was then dressed with sterile petrolatum gauze, bandaged, and taped.

DETD A rabbit was prepared for surgery and a full thickness of skin removed from an approximately square area 4 inches.times.4 inches. After spraying the area with sterile **alpha-keratose** ammonium keratinate solution prepared according to Example 1, a double-layered chitosan acetate sheeting similar to that employed in Example 12 was applied to the wound and surrounding skin. The area was then dressed with sterile petrolatum gauze, bandaged, and taped. A control wound of the same approximate size was also prepared, and was dressed only with sterile petrolatum gauze, bandaged, and taped. The wound sites were periodically examined for wound closure. During the first three weeks P.O., wound closure proceeded in the copolyelectrolyte hydrogel membrane-covered wound at a 50% faster rate than in the control wound.

DETD A goat was prepared for surgery, and full thicknesses of skin were removed from a rectangular area 8 inches.times.9 inches on one flank and from a rectangular area 7 inches.times.8 inches on the other flank. The smaller size wound was used as the control, and was dressed only with sterile petrolatum gauze, bandaged, and taped. The larger size wound was sprayed with sterile **alpha-keratose** ammonium keratinate solution prepared according to Example 1, overlaid with a double-layered chitosan acetate sheeting similar to that employed in Example 12, and then dressed with sterile petrolatum gauze, bandaged, and taped. The two wounds were examined periodically for wound healing and closure. After four days P.O., the copolyelectrolyte hydrogel membrane-covered wound was completely covered with fibroblasts, whereas the control wound showed no signs of healing. After 14 days P.O., the copolyelectrolyte hydrogel membrane-covered wound had closed 2 inches, while the control wound had closed less than 1 inch. After 66 days P.O., the hydrogel membrane-covered wound had been reduced to 1 inch .times.3 inches; whereas after 78 days P.O., the control wound had only closed to 2 inches.times.4 inches.

DETD Only the upper shallow pre-tibial lesion, most resembling the experimental surgical wounds produced in rabbits, was treated at first. The lesion was saturated with a sterile 5 mg/ml solution of

alpha-keratose ammonium keratinate prepared in a manner analogous to that of Example 1; thereafter a chitosan sheet [prepared as in the second paragraph of Example 5, but using 2 ml of glycerol] was laid down on the saturated wound surface. This was dressed with a Telfa pad [Kendall Hospital Products Div., Chicago, IL] and gauze. The chitosan sheet absorbed liquid keratinate to form a membrane which adhered to the wound. After 8 days, it was discovered that the wound was infected; the membrane was removed, the wound cleaned, and a chitosan keratinate copolyelectrolyte hydrogel membrane containing gentamycin sulfate prepared according to Example 6 was laid on the ulcer. Obvious success in treatment of the upper shallow ulcer led to gentamycin sulfate chitosan keratinate hydrogel membrane application to the other ulcers with comparable results. Treatment of the deep finger-like ulcer and the large cratered pre-tibial ulcer containing exposed tendon and a small area of exposed bone was then begun. The ulcers were saturated with a sterile 5 mg/ml **alpha-keratose** solution as above, then overlaid with a UV-sterilized glycerinated chitosan keratinate copolyelectrolyte hydrogel membrane containing gentamycin, prepared according to Example 6. The patient noted absence of tenseness and pain within minutes after the membrane was in place. From this day onward, pre-spraying of lesions with **alpha-keratose** was discontinued. Instead, the dried-down 9".times.12" chitosan acetate sheet was simply peeled from its container form, suspended in air by a set of clips, and sprayed on both sides with a total of 10 ml **alpha-keratose** (5-7.5 mg/ml) solution prepared according to Example 1, allowed to dry in air, then UV-sterilized under polyethylene (Saran Wrap) sheeting. After about 7 weeks a five-day-old membrane forming a firm carapace on the large lesion had split and lifted off of the healing site which was covered with collagenous fibrotic material. Exudate and drainage into the gauze overwrap was minimal. The patient was ambulatory, free of pain, and discharged from the hospital two weeks later. Follow-up treatment was on an out-patient basis at progressively longer intervals, where soft degraded or hardened non-adherent membrane was simply washed or cut away, the reduced lesion was washed in 3% peroxide, and a new gentamycin sulfate chitosan keratinate copolyelectrolyte hydrogel membrane prepared as above was applied and dressed as usual. Membrane degradation over the collagen-filled granulation base continued for two more months. "Pearling" at the edge of the lesion indicated new epithelial growth. Continued reduction of the lesion by epithelial ingrowth was apparent through the next 6 months to an uneventful recovery with complete reepithelialization.

DETD The patient was given a single course of amikacin/prostaphcillin therapy by intravenous drip. No surgical intervention took place. Simultaneously, therapy using 3% peroxide washes followed by application of chitosan keratinate/gentamycin copolyelectrolyte hydrogel membranes prepared according to Example 6 and the usual Telfa and gauze overwraps was initiated. Exudate-wet outer gauze wrapping was changed 2 or 3 times daily. Telfa pads and the chitosan keratinate/gentamycine copolyelectrolyte hydrogel membranes were replaced every 4 or 5 days following a peroxide wash with gauze pad swabbing to remove detritus. Only non-adherent membrane was removed or cut away. The patient was moved to a nursing facility within two weeks where glucosaminoglycan keratinate gentamycin copolyelectrolyte hydrogel membrane therapy was continued. The patient noted absence of pain with the membrane in place. Within 3 weeks the advent of fresh granulation tissue and sealing of the wound edges was apparent. However, continuing destruction of the devitalized tendon was apparent too. The tendon was soft and freely movable while the attending physician expressed pus for bacteriological studies. It was subsequently lifted and painlessly cut out. The Pseudomonas organism proved to be very sensitive to carbenicillin, and so two weeks after surgery the tendon-free lesion was cleaned with peroxide and swabbing, then covered with a gentamycin/carbenicillin-

containing chitosan keratinate copolyelectrolyte hydrogel membrane prepared according to Example 9. Carbenicillin-containing solutions polymerize directly and non-uniformly with the glycan solution. Membranes containing carbenicillin must therefore be formulated by spraying the chitosan acetate sheet (in this instance containing gentamycin sulfate) with **alpha-keratose** solution containing dissolved carbenicillin powder.

DETD With a second Pasteur pipette, the chitosan acetate-coated lumen of the tube was wetted with a solution of 5 mg/ml **alpha-keratose** solution prepared in a manner analogous to Example 1; the tubing was then allowed to dry again.

DETD In order to reduce thrombogenicity in the prosthesis, heparin sodium may be dissolved in the **alpha-keratose** solution used to wet down and bind the chitosan acetate component to the tube. (Heparin polymerizes directly with the chitosan acetate solution and therefore makes uniform dispersion in chitosan acetate solutions difficult).

CLM What is claimed is:

5. The copolyelectrolyte of claim 4, wherein the keratin moiety of said ammonium keratinate is **alpha-keratose**.

=> d his

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     (FILE 'HOME' ENTERED AT 13:31:49 ON 31 AUG 2002)
               DEL HIS
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 13:32:56 ON 31 AUG 2002
               E .ALPHA.-KERATOSE/CN
L1             1 S E3
L2             1 S ALPHA AND KERATOSE?
L3             1 S L1,L2

     FILE 'HCAOLD' ENTERED AT 13:34:58 ON 31 AUG 2002
L4             0 S L3

     FILE 'HCAPLUS' ENTERED AT 13:35:02 ON 31 AUG 2002
L5             9 S L3
L6           112 S (ALPHA OR ALFA)(S)KERATOSE
L7           114 S L5,L6
               E KERATOSE/CT
               E E3+ALL
L8            12 S E1(L)(ALPHA OR ALFA)
               E E2+ALL
L9             5 S E6
L10           11 S E4(L)(ALPHA OR ALFA)
L11          117 S L7-L10
L12           81 S L11 NOT TEXTILE?/SC,SX,CW
L13           28 S L12 NOT WOOL?
L14           18 S L13 NOT HAIR
L15            1 S L14 AND BLOOD
L16            2 S L11 AND BLOOD
L17            2 S L15,L16
L18            1 S L17 NOT HAIR
               E WIDRA A/AU
L19            7 S E3,E4
L20            3 S L19 AND L11
L21            3 S L18,L20
L22            4 S L19 NOT L21
L23            3 S L21 AND L5-L22
               SEL RN
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     FILE 'REGISTRY' ENTERED AT 13:40:58 ON 31 AUG 2002
L24            9 S E1-E9

     FILE 'HCAPLUS' ENTERED AT 13:41:24 ON 31 AUG 2002

     FILE 'BIOSIS' ENTERED AT 13:42:10 ON 31 AUG 2002
L25            1 S L3
L26           21 S L6
L27            2 S (ALPHA OR ALFA)()KERATOSE
L28           21 S L25-L27
                 E WIDRA A/AU
L29            7 S E3
L30            0 S L28 AND L29

     FILE 'EMBASE' ENTERED AT 13:45:32 ON 31 AUG 2002
L31            0 S L1
L32            0 S L27
                 E KERATOSE/CT

     FILE 'MEDLINE' ENTERED AT 13:46:07 ON 31 AUG 2002
L33            2 S L1 OR L27

     FILE 'DRUGLAUNCH' ENTERED AT 13:46:28 ON 31 AUG 2002
L34            0 S L27

     FILE 'BIOBUSINESS' ENTERED AT 13:47:03 ON 31 AUG 2002
L35            0 S L1 OR L27

     FILE 'CBNB' ENTERED AT 13:47:29 ON 31 AUG 2002
L36            0 S L27

     FILE 'DRUGU' ENTERED AT 13:50:20 ON 31 AUG 2002
L37            0 S L27

     FILE 'IMSDRUGCONF' ENTERED AT 13:51:11 ON 31 AUG 2002
L38            0 S L27

     FILE 'PHARMAML' ENTERED AT 13:51:52 ON 31 AUG 2002
L39            0 S L27

     FILE 'PHIC' ENTERED AT 13:52:04 ON 31 AUG 2002
L40            0 S L27

     FILE 'PROMT' ENTERED AT 13:52:31 ON 31 AUG 2002
L41            0 S L1 OR L27

     FILE 'WPIX' ENTERED AT 13:53:00 ON 31 AUG 2002
L42            6 S L27
L43            2 S L42 AND WOUND
L44            4 S L42 NOT L43
                 E R12587+ALL/DCN
                 E R01636+ALL/DCN
                 E R01655+ALL/DCN
                 E R01372+ALL/DCN
                 E 9822-B4501+ALL/DCN
                 E WIDRA A/AU
                 E E3
L45            2 S E3
L46            2 S L43,L45
L47            8 S (ALPHA OR ALFA)()KERATIN

     FILE 'WPIX' ENTERED AT 13:57:06 ON 31 AUG 2002
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     FILE''JICST-EPLUS, JAPIO' ENTERED AT 13:59:09 ON 31 AUG 2002
L48            2 S L27

     FILE 'USPATFULL, USPAT2' ENTERED AT 13:59:55 ON 31 AUG 2002
L49            0 S L1
L50           18 S L27
L51            5 S L50 NOT (HAIR OR SHAMPOO)/TI

     FILE 'USPATFULL, USPAT2' ENTERED AT 14:01:15 ON 31 AUG 2002
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